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Structural colour in colourimetric sensors and indicators

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Colourimetric sensors and indicators are widely used because of their low cost and simplicity. A significant challenge associated with the design of this type of device is that the sensing mechanism must be simultaneously optimised for the sensitivity of the response and a visually perceptible colour change. Structural colour, derived from coherent scattering rather than molecular absorption, is a promising route to colourimetric sensor design because colour shifts are tied to changes in one of many physical properties of a material, rather than a specific chemical process. This Feature Article presents an overview of the development of low-cost sensors and indicators that exploit structural colour. Building upon recent advances in structurally adaptive materials design, structural colour sensors have been developed for a wide variety of previously inaccessible physical (*e.g.* temperature, strain, electric fields) and chemical stimuli (*e.g.* small organic molecules, charged species, biomacromolecules and metabolites). These devices, often exceeding the state of the art in performance, simplicity or both, have bright prospects for market impact in areas such as environmental monitoring, workplace hazard identification, threat detection, and point-of-care diagnostics. Finding the ideal balance between performance (*e.g.* sensitivity, specificity, reproducibility, *etc.*) and simplicity (*e.g.* colourimetric *vs.* spectroscopic readout) will be one of the most critical elements in the further development of structural colour sensors. This balance should be driven largely by the market demands and competing technologies.

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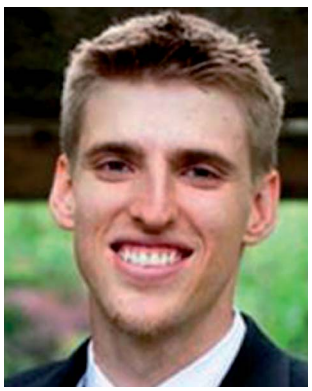
1 Introduction

There is a perpetual demand in society for new diagnostic devices, reflecting our never-ceasing thirst for greater knowledge of what is around us, what we are made of and what makes people sick. Most sensing platforms have common performance ideals, such as sensitivity, selectivity (resistance to false positives), simplicity



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(ease of use, cost *etc.*), and broad applicability of a technique or an approach. However, many of these qualities (*e.g.* sensitivity/specificity, generalizability and simplicity) generally are considered tradeoffs.[1] Perhaps most notable is the tradeoff between simplicity/cost and all of the performance ideals.[2–5]

A practical way to approach the problem of sensor design is to say "Given that I am willing to spend a fixed amount of money, time, and space on a sensing problem; how sensitive/specific can I make a sensor to address that problem?" For every level of simplicity, there is a range of applications (or customers) and a wide range of available technologies. For some applications, specificity and sensitivity are paramount and costs are tolerable. Examples of such applications are the analytical components of synthetic chemistry (*e.g.* pharmaceutical development) and lab-quality biochemical assays (*e.g.* for disease detection at a hospital).[6–8] For these problems, many highly sophisticated chemical analysis technologies have emerged, such as high-performance chromatography, mass-spectrometry, optical spectroscopy (FTIR, UV-Vis, *etc.*), nuclear magnetic resonance spectroscopy, high-resolution optical microscopy, electron microscopy, enzyme-linked immunosorbent assays, *etc.*[6–8]

On the other hand, there are many sensing problems where simplicity or low cost is the paramount ideal. This end of the sensor-design spectrum is the subject of intense research and development because many of these sensing problems are yet to have an elegant solution. Some examples of chemical sensing problems of this type are: detection of hazardous compounds in the field (*e.g.* at home, on the job, on the battlefield or at the airport),[9] medical diagnostics at home or in the developing world,[2–5] and authentication or quality control of consumer products (*e.g.* food, fuel, drugs, cosmetics, *etc.*) at home or in the field.[10] Despite usually being associated with a sacrifice in absolute performance (*e.g.* sensitivity or specificity), simple and low-cost diagnostic devices can be used both in more places and by more people, specifically by those who do not have sufficient resources and/or training to have access to the most sophisticated diagnostic technologies.[2–5]

Prof. Joanna Aizenberg is the Amy Smith Berylson Professor of Materials Science, Director of the Adaptive Material Technologies Platform at the Wyss Institute for Biologically Inspired Engineering, and the Director of the Kavli Institute at Harvard University. She runs a broad research program, covering biomimetics, self-assembly, smart materials, crystal engineering, surface science, biological and bio-inspired photonics. Aizenberg is an AAAS and APS Fellow, and is the recipient of an R&D 100 Award in 2012 and in 2013, the Fred Kavli Distinguished Lectureship in Nanoscience in 2009 and the Ronald Breslow Award for the Achievement in Biomimetic Chemistry in 2008.

Colourimetric sensing, where the readout is simply a change in an indicator's colour, is a particularly attractive approach to simple and low-cost diagnostics. With pH paper as a well-known example, colourimetric litmus tests have been widely commercially successful as a result of their low cost and accessibility.[11–13] However, expanding the use of colourimetric sensors has proved difficult. The challenge in designing a colourimetric sensor lies in finding a chemical process that couples strongly to both a specific target stimulus and to a visible colour change. Compounds that do meet these requirements (*e.g.* dyes whose absorption spectra vary with protonation/deprotonation[14]) tend to work only for specific types of stimuli (*e.g.* pH indicating), and are not readily generalizable to other sensing problems. The inherent chemical specificity of the colour change makes the generalization of this type of colourimetric sensing to most other types of measurements difficult.

One approach to developing a broadly generalizable platform for colourimetric sensing is to identify a type of colour change that can be induced by a very generic, chemically non-specific mechanism. For each application (*e.g.* detection of glucose in blood serum), we can then add a chemically specific link between this generic colour-change mechanism and the desired unknown stimulus or specific analyte.

Exploiting structural colour for sensing exemplifies this approach, and is a promising route to broadly expanding the availability of colourimetric sensors. Structural colour derives from light scattering rather than absorption, and as the name sounds, is most sensitive to changes in the structure of a material rather than specific chemical processes.[15] Bright structural colour at visible wavelengths is associated with roughness or porosity on the wavelength scale that possesses some degree of spatial coherence (order).[15,16] Structural colour is readily tuned by any mechanism that tunes the scattering profile of the structure (*e.g.* changes in size, aspect ratio, shape, refractive index, or the degree of spatial coherence, *etc.*).[17–36] These changes are all associated with *physical* properties of a material forming the structure, and do not rely on a specific *chemical* state responsible for molecular absorption. Since the colour changes are no longer bound to any one specific material or chemical process (the only requirement being that the material is heterogeneous, rough or porous on a scale that is comparable to the wavelengths of visible light), the chemical composition of the material forming the structure is a degree of freedom that can be tailored to impart colourimetric sensing capability to a particular stimulus.

In this Feature Article, we will highlight recent progress in the development of colourimetric sensors based on tunable structurally coloured materials. To design a structural colour sensor one must: (1) synthesize a material that undergoes structural changes in response to the desired target stimulus, and (2) nanotexture that material to produce a tunable colour readout. In the following sections we overview strategies to make structural colours and to engineer their response to a variety of physical and chemical stimuli. While exploiting adaptive plasmonic responses is also a promising route to the design of spectroscopic and colourimetric sensors, this is beyond the scope of this article. We direct the reader instead to several prominent reviews on this topic.[37–40]

2 Patterning a material to be structurally coloured

Structural colour derives from enhanced scattering of particular spectral regions as opposed to absorption of light from a pigment. Light is scattered at interfaces between materials of differing refractive index. Many objects that we encounter in everyday life contain small inhomogeneities that scatter light (milk and clouds are two examples). If the size and spacing of these scattering centers are randomised, a white colour is typically observed, as all wavelength regions are scattered with equal efficiency. However when there is a wavelength-scale degree of spatial coherence between the scattering centers, constructive interference between scattered waves results in wavelength-specific enhancements of reflection and the appearance of colour. While there exist a vast range of functional materials in which dynamic structural changes can be induced (as will be described in Section 3), essential to the design of such a platform is a means to impart wavelength-scale structure to these materials in order to produce colour. Fig. 1 shows schematics of several examples of structures that produce structural colour, structured in one, two or three dimensions.

A single thin film or etalon is one of the simplest structures that can produce colour from coherent scattering. Colour results from interference between reflections from the upper and lower interfaces.[20] Periodic multilayers of thin films, depicted in Fig. 1 (left), provide enhanced strength of the Bragg reflection peak. A spectral photonic bandgap (total reflection) exists for ideal structures with infinite periods and requires a smaller number of layers to achieve complete reflectivity as the refractive-index contrast increases. Thin films and multilayers are readily fabricated through a number of standard laboratory protocols, such as spin casting, atomic layer deposition, molecular-beam epitaxy or chemical vapour deposition.[16,41]

1D and 2D diffraction gratings, depicted in Fig. 1 (center), are also used to make structural colours. Lateral periodicities required to produce strong diffraction in the visible range are large enough to be patterned with photolithography.[42] While lithography and etching can be used to pattern many types of stimuli-responsive materials, soft-lithography techniques (*e.g.* replica molding, printing, imprint lithography[43]) are very versatile and scalable for patterning soft materials. 2D and 3D periodic photonic structures can also be fabricated in a scalable manner using interference lithography, holographic lithography[44–46] and two-photon lithography.[47]

Colloidal self-assembly is one of the most versatile techniques to template structural colours in a wide range of adaptive materials.[20–26] In this approach, a wavelength-scale periodic structure is formed by the self-assembly of monodisperse colloidal particles from a suspension into a close-packed lattice. Monodisperse suspensions of colloidal microspheres are most commonly made of polystyrene (PS), polymethylmethacrylate (PMMA), or silica with sphere diameters that can be readily controlled from synthesis conditions to be anywhere from tens of nanometers to several microns, allowing the colour (due to the wavelength-region of strongest Bragg reflection) of the structure to be tuned.[20–26] This self-assembly process can be induced in a variety of ways (*e.g.* sedimentation, centrifugation, evaporation, confinement *etc.*).[20]

Colloidal photonic crystals can be used directly as structural-colour sensors when the spheres are composed of a responsive material.[48] Alternatively, the interstitial sites of the close-packed arrays can be infiltrated with a functional material.[49] Colloidal-crystal assembly and infiltration is most commonly done as a two-step process, however co-assembly of a colloidal crystal and an interstitial matrix has been shown to improve structural order in addition to increasing simplicity of fabrication.[50] After infiltration, the original colloidal crystal template can be removed (either by chemical etching or pyrolysis), leaving behind an inverse-opal, depicted in Fig. 1 (right). This can be done either to increase the refractive-index-contrast, or to open up porosity in the structure.[20]

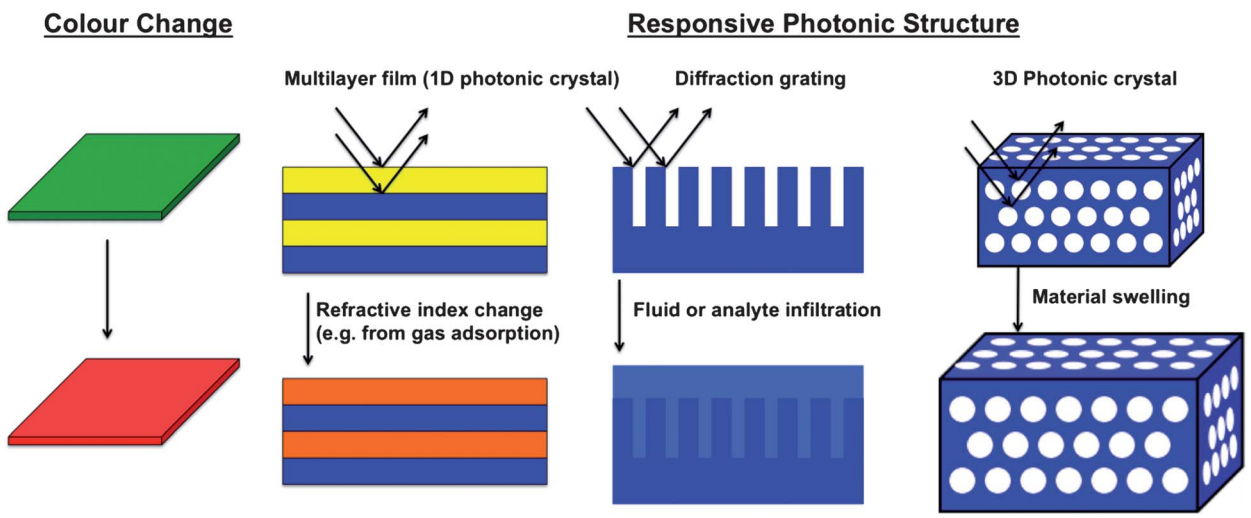

Fig. 1 Schematics of common types of structural colours with examples of tuning mechanisms. (Left) Multilayer thin films (1D photonic crystals), (center) diffraction gratings, (right) 3D photonic crystals. Colour can be tuned by any mechanism that alters the optical path length between interfaces, such as (left) refractive index changes in one or more components, (center) infiltration of fluid or analyte into porosity in the structure, or (right) structural expansion from material swelling.

Table 1 Summary of routes to achieving structural colour response to several different physical, chemical and biochemical stimuli

Stimulus/analyte	Actuation mechanism(s)	Estimated colourimetric sensitivity
Mechanical strain	Elastomeric photonic structures[27,52,53]	5–10% strain
Heat	Structured hydrogels with temperature response[48,59–64]	Temperature changes of 1° (near hydrogel transition temperature)
Electric fields	Oxidation/reduction in structured polyelectrolyte gels[66]	Voltage changes of ~200 mV (ref. 66)
Small molecules (vapour)	Gas adsorption in mesoporous Bragg stacks and photonic crystals[35,80] or porous silicon photonic crystals[81–83]	$P/P_0 \sim 0.1$ (ref. 84)
Humidity	Photonic crystals incorporating hydrophilic swellable polymers or hydrogels[86,87,89–91]	20% R.H.[91]
Organic liquids	Wetting in inverse-opal photonic crystals[93–95]	Intrinsic contact angle changes of ~3° (*e.g.* 2.5% change of alcohol concentration in water)[94]
	Liquid uptake in mesoporous Bragg stacks,[77,79] swelling in hydrogel photonic crystals[92]	*E.g.* 10% change of alcohol concentration in water[92]
Metal ions in solution (Pb^{2+}, Na^{+}, K^{+})	Hydrogel photonic structures containing metal-binding ligands[108]	4 ppm (ref. 108)
pH	Hydrogel photonic structures with pH-responsive groups (*e.g.* acrylic acid)[118–121]	pH changes on the order of 1 pH unit[121]
Glucose	Structured hydrogels containing glucose-binding moieties[109,122–130,135–137]	1 μM in synthetic tear fluid[135]
Other small biomolecules (carbohydrates,[131,132] creatine,[133] cholic acid,[102] cholesterol[101])	Hydrogel photonic structures containing analyte-binding ligands or molecularly imprinted photonic hydrogels[100–102,131–133]	0.1 mM (creatine[133]), 50 μM (simple carbohydrates[131]), $<10^{-10}$ M (cholic acid[102])
Biomacromolecules (*e.g.* proteins, DNA)	Adsorption in porous silicon thin films and multilayers[138–149] and inverse opals,[151–153] volume change in photonic structures made from bioresponsive hydrogels[153,154]	$<10^{-8}$ M (ref. 138)

3 Engineering stimulus response

With many nanofabrication techniques available to structure all types of materials, the development of structural colour sensors for a given stimulus has followed the development of responsive materials that undergo structural changes in response to that stimulus. In this section, we describe structural colour sensors that have been developed to detect or measure physical stimuli (*e.g.* temperature, strain, electric fields) and chemical stimuli (*e.g.* small molecules, charged species, biological molecules and metabolites). Table 1 summarizes several approaches developed to colourimetrically detect these stimuli that are described in this section.

3.1 Physical stimuli

There are numerous materials that undergo deformation in response to a variety of stimuli. These have formed the basis for structural colour platforms for sensing these stimuli. Elastomeric materials, such as silicone rubber, have been used by several groups to make structural colours that tune in response to mechanical strain.[27,52,53] Kolle *et al.* built structurally coloured sheets[52] from 1D photonic-crystal films of alternating polydimethylsiloxane (PDMS) and polystyrene-*co*-polyisoprene (PS/PI) layers (Fig. 2). By rolling up these sheets, they also made colourimetrically strain-sensitive fibres.[53] Fibres with strain-sensitive colour have several promising applications in areas such as colour-responsive textiles.

Sheets of strain-sensitive structural colours have also been made by incorporating an elastomer into a colloidal crystal. Arsenault *et al.*[27] created porous elastic inverse-opals by polymerizing cross-linked alkylmethacrylate elastomers around close-packed silica beads before removing the template with hydrofluoric acid. Other groups have infiltrated opals of polymer or silica nanospheres with elastomers without removing

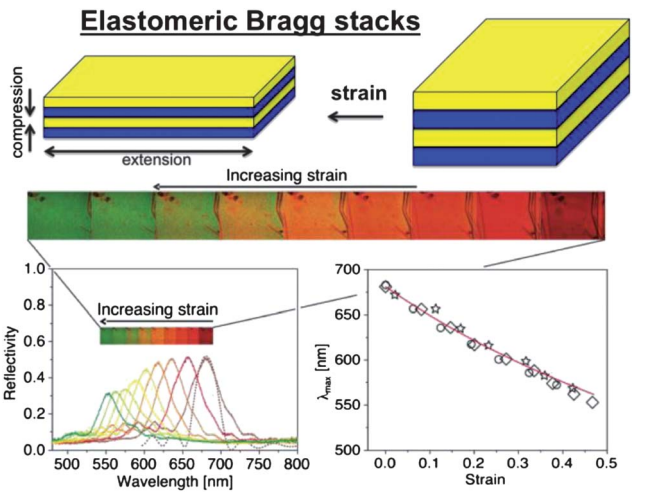

Fig. 2 Strain-responsive structural colour from elastomeric Bragg stacks. Reproduced with permission from ref. 52. Copyright 2010, the Optical Society of America.

the template, achieving similar tuning ranges.[30,51,54–56] Colour fingerprinting is one of the possible applications for these materials.[27] For strain-responsive structural colours, the percentage shift in the reflectance peak ($\Delta\lambda/\lambda_0$) will on the order of the percentage strain in the structure.[53] Therefore, it takes strain on the order of 5–10% to produce colour changes that are easily visible to the naked eye.

There are several ways to make temperature-responsive structural colours. Kubo *et al.* also achieved temperature responsive colour by infiltrating SiO_2 inverse opals with a nematic liquid crystal.[57] Thermally induced phase changes in the liquid crystals were associated with substantial changes in the refractive index, which altered the optical path length of the structure's periodicity.

Hydrogels can also be used as a basis for temperature-responsive colour.[58] Hydrogels are a versatile class of materials that are widely used in structural colour sensors. Hydrogels undergo large reversible volume changes from water uptake and expulsion. By engineering the functional groups in a hydrogel matrix, volume changes can be tuned to a wide variety of physical and chemical stimuli. Poly(*N*-isopropylacrylamide) (PNIPAAM) hydrogels undergo temperature-responsive volume-phase transitions. By adding different functional groups to the polymer backbone, the transition temperature can be tuned. A pioneering demonstration of hydrogel-actuated structural colour, Weissman *et al.* infiltrated an opal of polystyrene (PS) spheres with PNIPAAM[58] forming a photonic crystal whose colour was temperature responsive. Since then several other groups have built temperature-responsive colours based on PNIPAAM in opal and inverse-opal structures[48,59–63] as well as other geometries.[64]

Structurally coloured materials with electrical tunability are promising for applications in both colourimetric sensing and reflective display technology. Arsenault *et al.* designed an electric-field-responsive photonic composite based on a silica opal infiltrated with polyferrocenylsilane (PFS).[65,66] The PFS undergoes an electrochemically driven swelling and shrinking in an electrolyte solution, tuning the periodicity of the silica particle lattice and thus the reflectance peak. Using this structure, they demonstrated tuning over the full range of visible wavelengths. Magnetically tunable structurally coloured materials have also been made from ordered arrays of colloidal magnetic particles, both in solution and in a polymer matrix.[32,67–69]

3.2 Chemical stimuli

The global non-military market for chemical and biosensors accounts is over $10 billion annually and fulfils important functions in society such as disease diagnosis, health and safety monitoring, threat and hazard detection, and industrial quality control.[70] Portable and low-cost sensors create new markets for these devices where current needs are unmet, expanding the use of lab-quality testing to more people (*e.g.* users with little training) in more places (*e.g.* the field, the home and resource-poor environments). Structural colour has been used to develop colourimetric sensors for many types of applications where they did not exist.

3.2.1 Small organic molecules. There is a ubiquitous demand for devices that can detect and identify small molecules. Health-monitoring and disease diagnosis frequently require tracking the levels of sugars and metabolites in bodily fluids. Identification of particular small molecules also plays an essential role in environmental monitoring and security screening. Structural colour sensors for small molecules most commonly operate through adsorption (from vapour) or uptake (from solution) of these compounds into the structure, resulting in a change in the optical path length, either through physical swelling or changes in the material refractive index. Adsorption of vapours is known to cause significant refractive index changes in solids with high porosity on a sub-wavelength scale.[71] Consequently, photonic structures built from these materials display reflectance peaks that shift with vapour adsorption.

The refractive index of mesoporous materials, with high porosity on a ~1–10 nm scale, can be tuned over a wide range with even a monolayer adsorption of small molecules from vapour, due to the exceptionally high surface area/volume ratio in this class of materials.[71] Mesoporous materials can be built from nanoparticle suspensions (*e.g.* by spin-casting),[35] or from sol–gel growth of inorganic materials in the presence of surfactants[72,73] or liquid-crystalline phases.[74] Porosity on this scale can also be formed by etching initially non-porous materials.[75] Any type of photonic structure built from mesoporous materials will exhibit photonic properties that tune in response to vapour adsorption[35,76] or liquid infiltration.[77]

Porous Bragg stacks built from alternating SiO_2 and TiO_2 nanoparticle layers made colourimetric sensors that produced bright colours and could be fabricated simply from spin-coating.[77–80] When infiltrated with liquids, the reflectance peak shifted in response to the chemistry and refractive index of the liquid[77,79] (Fig. 3A and B). For compounds belonging to a common family (*e.g.* alcohols, alkanes) linear responses were observed in correlation with the liquid refractive index at a slope of ~100 nm RIU^{-1} (1 nm/0.01 RIU). However, the baseline shift was found to be different depending on the class of compounds

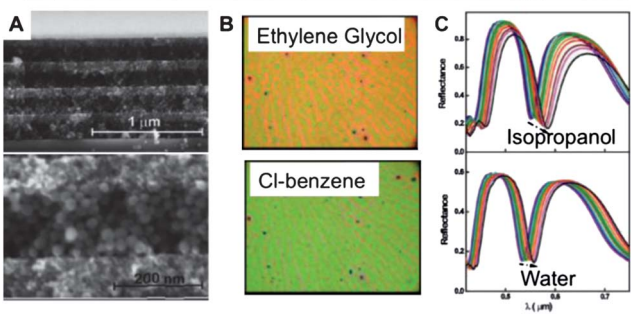

Fig. 3 (A) Scanning electron micrographs of porous SiO_2/TiO_2 nanoparticle Bragg stacks. (B) Colourimetric response liquids with different refractive indices. (C) Redshift of the reflection profile of a Bragg stack with a planar defect (cavity) in response to different partial pressure of isopropanol (top) and water (bottom) with partial pressures ranging form 0–1. Reproduced with permission from ref. 79 (A and B) and 80 (C). Copyright 2008, the American Chemical Society.

(*e.g.* alcohols *vs.* alkanes), indicating a degree of chemical selectivity to the uptake of liquids.[77,79] Similar results were also observed for gas adsorption (Fig. 3C).[35,80] Functionalization of the pore surfaces after fabrication of the Bragg stacks facilitated adjustable affinity to particular classes of molecules and improves the chemical specificity of sensors.[35] Porous silicon photonic crystals have also been used as diffractive optical elements for gas detection.[81–83] Surface functionalization of these structures is readily done using silane chemistry, imparting a degree of specificity to the responses. These materials were shown to be effective indicators for monitoring the service life of activated carbon respirator filters.[82]

The colourimetric sensitivity to gas uptake is generally fairly limited in porous photonic structures, since the relative peak shift is in proportion to the relative amount of material that has adsorbed, and significant peak shifts are required for a visible colour change. This limits colourimetric detection of gases to concentrations at or above ($P/P_0 \sim 0.1$) in typical implementations.[84] Spectroscopy[84,85] or digital image analysis[35] can both be used to improve sensitivity by several orders of magnitude, but require higher costs and access to power to implement. Potyrailo *et al.*[84,85] showed that differential spectroscopy on both natural (scales of the butterfly *Morpho sulkowskyi*) and synthetic structurally coloured materials (core–shell opals) allowed for detection of gas adsorption with high sensitivity and chemical specificity. Different types of vapours were distinguished using multivariate analysis on several wavelength components of the spectral signals.

1D Bragg stacks[86,87] and colloidally templated 3D photonic crystals[30,88] made from swellable polymers also provide a platform for colourimetric detection of simple compounds. Similarly, the water-swelling nature of hydrogel photonic crystals allows them to serve as humidity sensors.[89–91] Hydrogel photonic crystals can also offer selective swelling response to other hydrophilic compounds such as alcohols.[92]

Wetting has also been used as a basis for a structural indicator for identification of organic liquids (Fig. 4).[93–95] It was shown that chemically functionalised silica inverse-opal films possess a highly selective wettability threshold for liquid infiltration.[93] Infiltration was associated with a disappearance of the structure's iridescent colour due to refractive index matching of the liquid and the matrix. When the surface chemistry was spatially patterned in these structures, liquids could be identified through characteristic spatial patterns of wetted and non-wetted regions.[93,94] This technique has the advantage that detection is based on *counting* empty (coloured) and filled (dark) regions, rather than measuring small colour changes (that are also generally angle-dependent), producing readings that can be unambiguously decrypted by an untrained user. Another group has combined wetting and hydrogel responses in functionalised inverse-opal hydrogels and demonstrated low-level detection of several different types of surfactants.[96,97]

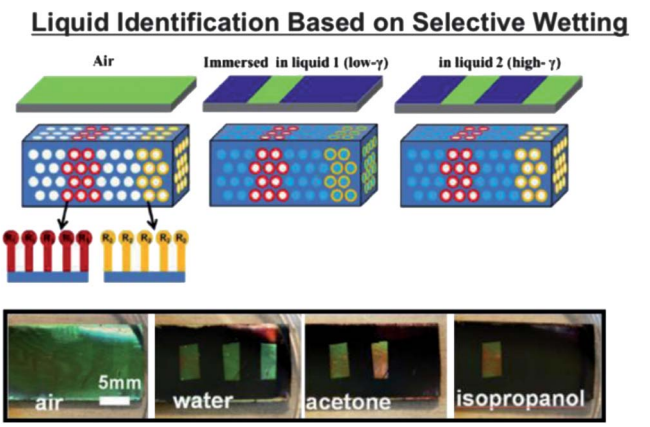

Fig. 4 Colourimetric differentiation of liquids based on selective wetting in an inverse-opal 3D photonic crystal with spatially patterned surface chemistry. Reproduced from ref. 93 with permission. Copyright 2011, the American Chemical Society.

Identifying simple compounds with chemical specificity is a significant challenge in the development of structural colour sensors and indicators, particularly for small molecules. Colourimetric responses based on generic physical processes such as adsorption, swelling and wetting have the advantage of broad applicability to the detection of many different types of simple compounds. However, there is an inherent trade-off between the breadth of applicability of a sensor and its specificity. With many possible identities of an unknown, a single indicator has the ability to probe a single property of the sample. A single, very specific test (*i.e.* using an antibody or aptamer to identify a specific biomarker) can be sufficient to identify the unknown in the event of an affirmative response. For applications where really only one possible identity matters (*e.g.* diagnosis of a specific disease), this approach is ideal. Molecular imprinting is emerging as a promising route to engineering polymers with specific responses to small organic molecules.[98–101] Early demonstrations of structural colour sensors based on molecular imprinting have emerged, with the detection of cholic acid[102] and bisphenol-A.[103] Chiral recognition in photonic polymers using molecular imprinting has also been demonstrated.[104]

Lock-and-key sensors become impractical where correct identification of an unknown from a broad list of possibilities is desired, since a negative response yields relatively little information. To be able to deterministically identify an unknown form a list of n possibilities using this approach, one has to develop $(n - 1)$ highly specific sensors. A more effective approach to correctly identify an unknown from a broad list of possibilities is to perform a series of general tests, the combination of which produces highly specific information in all possible outcomes.[1,35,95,105,106] Combinatorial recognition of substances is the strategy employed by our olfactory system[1] and thus many combinatorial sensing platforms are referred to as "artificial noses". The key to maximizing specificity using the fewest possible tests in this approach is to ensure that the tests are highly independent of one another.

Bonifacio *et al.* has applied combinatorial sensing to vapour identification using porous silica/titania Bragg stacks.[35,107] Nine Bragg stacks, each surface-functionalised with a different alkoxysilane, were used as the sensor array. Notably, they replaced traditional spectroscopic measurements with RGB analysis of images from a digital camera in an illumination chamber with the sample, an approach that may prove more robust and scalable. Using combinatorial analysis of the

images, their "photonic nose" was able to successfully differentiate several different organic liquids, metabolites from different bacterial species[35] and ageing conditions for different types of meat.[107]

We recently applied this combinatorial approach to our wetting-based colourimetric indicator for liquids.[95] We created an array of six indicators, each employing a vertical wettability gradient designed to exhibit non-trivial (*i.e.* partially wetted) responses over a broad common range of organic liquids (*e.g.* surface tension of ~20–30 mN m^{-1}), but with distinct types of surface groups used in each. Counting coloured regions and comparing them to the response of the elements to reference mixtures of water and ethanol quantified responses. This array was able to mutually distinguish a set of 15 common solvents. It was also able to make predictions about the chemical properties of previously uncharacterised substances (*i.e.* not in a given library) by comparing it to known compounds.

3.2.2 Detection of charged species and pH. Monitoring the presence and quantity of charged species in aqueous solution is important for food and water quality monitoring as well as in the diagnosis and tracking of certain diseases. Incorporating responsive gels into iridescent structures has proven to be highly effective for colourimetric detection of charged species in solution. Holtz and Asher first demonstrated the detection of Pb^{2+}, Ba^{2+}, K^{+} ions in solution using a colloidal 3D photonic crystal encapsulated in a hydrogel that contained metal-binding crown ether moieties.[108] Binding of metal ions by the gel immobilises them, creating an osmotic pressure within the gel that increases its volume and, in turn, redshifts the reflection maximum. Spectral shifts were easily detectable for Pb^{2+} concentrations below 100 ppb and were visible to the naked eye at concentrations as low as 4 ppm.[108] Quantifiable responses were observed over 5 orders of magnitude of Pb^{2+} concentration before saturation of the crown ether groups occurred. In the subsequent decade and a half, structured ion-binding and polyelectrolyte gels have been adapted to colourimetrically analyse a large variety of charged species.[109–116]

The Asher group recently showed that diffraction efficiency and colourimetric sensitivity were improved using a 2D photonic crystal design, consisting of a close-packed colloidal monolayer embedded in a hydrogel film on a highly reflective substrate.[117] The reflective substrate greatly enhances the reflective colour, allowing 80% of the light to be diffracted. The 2D nature of the film also provides the hydrogel with improved access to analytes in solution.

Structured hydrogels have also been used to create colourimetric pH sensors in several different geometries, from planar micorgel etalons[118] to colloidally templated hydrogel opals and inverse opals.[119–121] The protonation or deprotonation of pendant groups in the gel matrix induces volume changes due to the ionization of the gel. For a given type of pendant group, sensitivity is greatest near its pK_a.

3.2.3 Biosensing. Medical diagnostics is an important area for the development of new sensors and indicators. In particular, there is an increasing demand for point-of-care diagnostics that can be used in the field or at home.[2,36] The design of point-of-care diagnostics for medicine provides many challenges that are difficult to address with a simple technology. Identification and quantification of a given biomarker from a sample of biological fluid is similar to trying to count a handful of needles in a haystack, requiring an exceptional degree of sensitivity and specificity in the presumed absence of sophisticated sample preparation techniques. Using structural colour for biomolecule detection eliminates the need for labelling, offering both a significant reduction in the complexity and cost of a sensing protocol and an opportunity to track kinetic properties of the targets in their native state.[36] While some highlights of the development of structural colour biosensors will be overviewed here, we also direct the reader to ref. 36 for a recent detailed review on the use of photonic crystals for biosensing.

One of the early successes of structural colour sensors in biomedical areas has been the detection of glucose. With the incidence of diabetes growing rapidly in the developed world,[36] demand has been growing for simple and effective glucose monitors suitable for the home. Holtz *et al.*[109] first demonstrated a colourimetric glucose sensor based on a 3D photonic crystal hydrogel, containing the bound enzyme glucose oxidase. Structured hydrogels containing this and other glucose-binding moieties have since been demonstrated in a variety of geometries including opaline 3D photonic crystals,[122–127] metal-doped hydrogel diffraction gratings,[128,129] and metal-capped hydrogel Fabry–Perot etalons.[130] These techniques have also been extended to detect other types of small biomolecules, such as carbohydrates,[131,132] creatine[133] and cholic acid.[102]

Structural colour hydrogel glucose sensors are some of the first biomedical structural colour sensors to find clinical application[36] and have been shown to work at levels clinically relevant for human blood serum[134] and tear fluid.[135–137] The latter platform,

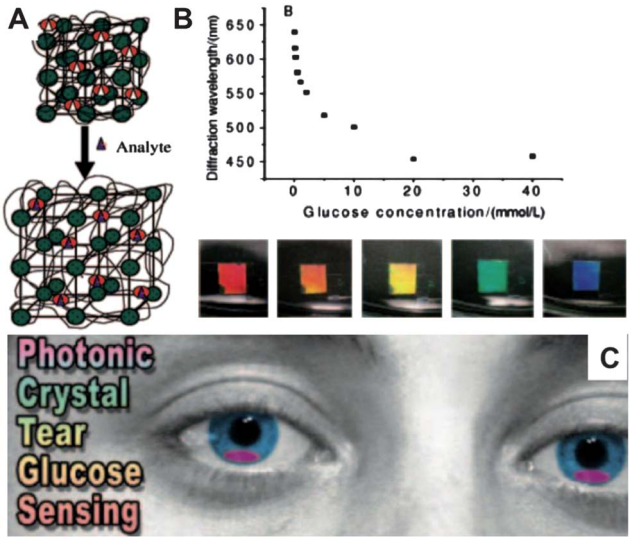

Fig. 5 Colloidal 3D photonic crystal contained in a hydrogel matrix for sensing low glucose concentrations in tear fluid. (A) The hydrogel matrix contained 4-amino-3-fluorophenylboronic acid groups that bind glucose, inducing gel swelling. (B) Diffraction peak shift (top) and colour change (below) in response to different glucose concentrations, showing maximum colourimetric sensitivity below 10 mmol L^{-1} in artificial tear fluid. (C) Drawing depicting potential use in an ocular insert or contact lens. Reproduced from ref. 135 with permission. Copyright 2004 American Association for Clinical Chemistry.

depicted in Fig. 5, is particularly attractive for glucose monitoring because it can be implemented in a highly non-invasive manner, either as an ocular insert or in contact lenses.[135–137]

Dynamic reflectance peaks from porous silicon thin films[138] and 1D photonic crystals (multilayers)[82,139] have been used as label-free sensors for a wide variety of biological species, including small molecules (*e.g.* biotin), DNA oligomers and proteins.[138–149] In this geometry, analyte binding within the sub-wavelength pores induces changes in the effective refractive indices of the layers, producing detectible changes in the reflectance peak. Sensor specificity can be improved by functionalizing the pore surfaces with specific binding agents (*e.g.* complementary DNA, antibodies, molecular recognition agents),[140–146] tuning the multilayer structure to create sharper reflectance peaks[147,148] and by tuning the pore size to restrict access to only analyte molecules with certain size.[149] The ability to sort analytes by size makes porous silicon films and Bragg stacks also useful for real-time monitoring of biochemical processes associated with a change in molecular size (*e.g.* protease activity).[150]

Protein detection based on adsorption was also demonstrated in inverse-opal films made of polymer[151] and inorganic materials.[152] Here the porosity derived from the colloidal crystal template serves as both the source of the iridescent colour and the high surface area for protein adsorption. Protein adsorbed onto the pore surfaces increased the optical path length of periodicity with sufficient magnitude for spectroscopic detection.

Photonic crystals built from bioresponsive hydrogels show increased sensitivity to binding by adding the effect of volume changes to the uptake of analyte.[36,153,154] In addition to the glucose-responsive gels discussed above, hydrogels with selective responses to DNA oligomers and specific proteins have also been developed[153,154] and implemented into tunable photonic crystals.[155,156] Hydrogel response to biomolecules can be engineered through a variety of mechanisms (see Fig. 6), such as the formation of cross-links from gel-bound ligands and analyte molecules, the cleaving of gel cross-links by an active analyte molecule (*e.g.* enzyme), and other types of reactions between bound species in the gel matrix and analytes (*e.g.* enzyme–substrate reactions).[154]

Most biosensors based on dynamic structural colour rely on spectroscopic readouts rather than visual colour change to determine the response. Although this increases sensor complexity, photonic biosensors provide a number of performance advantages compared to other competing technologies at similar costs. They facilitate label-free detection and are compatible with a larger variety of material platforms than approaches based on surface plasmon resonances, improving their prospects for biocompatibility. They can also be made from materials that are biodegradable and suitable for implantation in the body.[154]

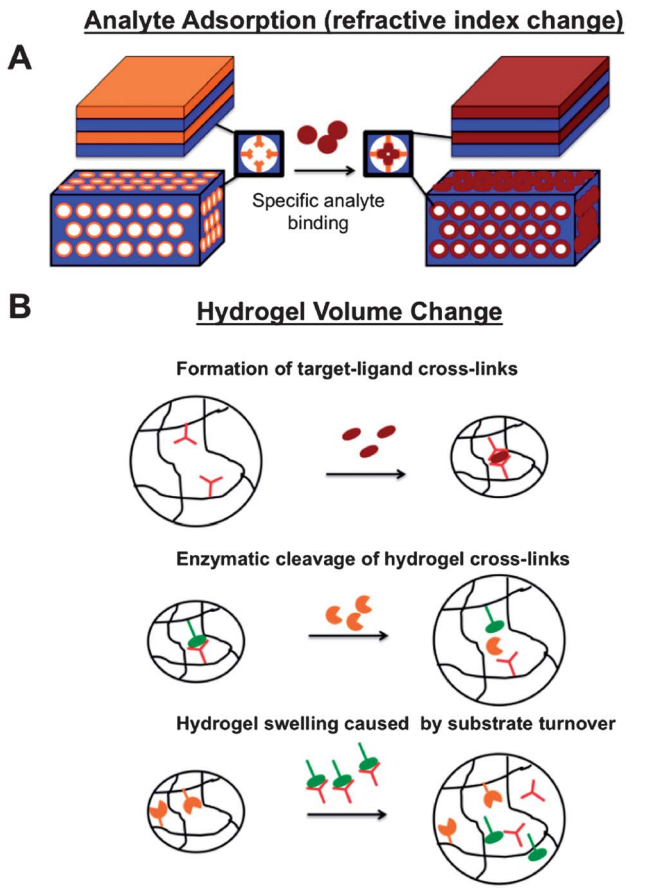

Fig. 6 Schematics depicting different mechanisms that have been exploited in the design of structural colour biosensors. (A) Analyte binding to the walls of porous photonic structures, such as mesoporous multilayers or inverse opals, can cause refractive index changes of sufficient magnitude to tune the colour of the structure.[138–152] (B) Schematic showing several routes to bio-responsive hydrogel volume changes (see ref. 153–156).

4 Challenges

4.1 Specificity

As structural colour responses operate based on changes in physical properties of a structure such as shape or density, rather than specific chemical processes, they have expanded the variety of physical and chemical stimuli that can be detected colourimetrically. However, the reliance on structural changes also makes engineering responses that are specific to only one stimulus more challenging. This is a challenge that is prevalent in structural colour sensors for both physical and chemical stimuli.

Researchers have already begun to explore several approaches to increasing specificity for several of the colourimetric sensing technologies mentioned here. Approaches generally fall into one of two categories, based on (i) lock-and-key detection, characterised by highly specific targeted response to a single stimulus,[36,98–104] and (ii) specificity through combinatorial response of an array of sensors that each have weak specificity.[1,35,95,105] Lock-and-key approaches based on highly specific ligand binding or molecular imprinting in structurally responsive surfaces or polymers are ideal for applications where low levels of a particular analyte need to be isolated from a noisy chemical environment. This approach seems particularly promising for many medical applications. Combinatorial approaches are more ideal for determining physical properties and overall composition of a mixture and monitoring their evolution.[35,95] These approaches may be very useful for applications such as food quality monitoring.[107]

4.2 Maintaining simplicity: visual perception of colour *vs.* spectroscopy

The balance between performance and simplicity in the design of sensors and indicators is of paramount importance because it determines the applications for which a new technology is a viable improvement over other pre-existing technologies. The use of colour as a readout makes structural colour sensing platforms promising for applications where simplicity is required and power is not accessible. However, maintaining the simplicity in these sensors is challenging in practice. In the vast majority of the colourimetric sensors studied in this article, spectroscopy was actually used to quantify the responses. Requiring spectroscopy to make a measurement adds significantly to the cost, equipment and power requirements of a sensor, and removes many of the advantages associated with colourimetric technologies over other possible solutions. On the other hand spectroscopic readouts can significantly increase the sensitivity and specificity of these sensors, making them competitive even with more complex analytical techniques in some cases.[35,85]

It is not always straightforward to translate the spectral responses from dynamic structural colours into colour changes that are unambiguously readable by eye. One reason is that structural colours generally vary strongly with both lighting and viewing angles, both of which are difficult to reproduce in a controlled way in the field. Furthermore, the dependence of colour on material structure rather than the presence of a particular absorber makes the initial and final apparent colours more sensitive to fabrication variations and harder to reproduce.

There are several simple modifications that can be made to many types of structural colour sensors to make outputs easy to read, while enhancing the reproducibility of readouts. For example, users could be given a direct reference for comparison. One simple way to accomplish this would be to restrict responsiveness to only a portion of a coloured film (*e.g.* by masking a portion with a transparent barrier). In this approach, colour changes would be recognised by the appearance of shapes built from between the actuated and non-actuated regions (*e.g.* Fig. 4 (ref. 93)). Recognizing signal from colour contrast and the appearance of interfaces rather than absolute colour makes unambiguous signal detection angle-independent, but only does so in a digital fashion (*i.e.* either there is a signal or there is no signal). Furthermore, this approach makes use of an internal standard, enhancing the robustness of the sensor against fabrication imperfections. Making this type of a digital output (*i.e.* that can be quantified by counting or measuring shapes rather than comparing colours) out of a multi-level or continuous-scale response can be more difficult in certain types of structural colour sensors, but can be readily accomplished in others.[93–95] Add-ons to structural colour sensors that limit the viewing angles can also be used to decrease the ambiguity of the response. Limiting the viewing angle could make comparison with a printed reference card more practical in the field.

4.3 Commercialisation

Using structural colour as a basis for sensing greatly expands the range of stimuli that can be colourimetrically detected. As a result, structural colour sensors should make more inroads into the marketplace in the coming decade. However, commercial success for these technologies hinges on how well they can compete with currently available solutions. Successful products must address a market where there is a strong demand and surpass the state of the art in absolute performance, simplicity or both. There is greater potential impact in certain applications over others. For example, colourimetric pH sensors based on structural colour face a market that already contains effective technologies for both low-cost in-field applications (pH paper) and higher precision techniques (pH meters).

Point-of-care diagnostics may be one of the most promising markets for structural colour sensors. The point-of-care testing market is expected to grow to $25 billion by 2016, and with the increasing incidence of diabetes in the developed world, blood glucose monitoring accounts for around 70% of this market.[157] Colourimetric glucose monitors based on photonic-crystal hydrogels show promise as minimally invasive ocular inserts,[135–137] and have formed the basis for several startup companies to date.[36]

5 Summary and outlook

In this Feature Article, we have presented an overview of the development of structural colour devices for low-cost sensors and indicators. By relying on structural changes for responsive colour as opposed to specific chemical processes, colourimetric sensors have been developed for a wide variety of previously inaccessible physical and chemical stimuli and have bright prospects for implementation in several markets, such as point-of-care diagnostics, environmental monitoring, workplace hazard identification, and threat detection. Negotiating the tradeoff between performance (*e.g.* sensitivity, specificity, reproducibility, *etc.*) and simplicity (*e.g.* colourimetric *vs.* spectroscopic readout) is the greatest challenge in the design of new structural colour sensors and is critical to their commercial success. An ideal balance of the two parameters should be determined by both the market demands and the available competing technologies.

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